Remarks

Claims 1, 4-5, 8-9, 12-24 and 26-27 are pending in the application. Applicants have amended the claims to overcome the rejections under 35 U.S.C. §112, first paragraph and 35 U.S.C. §103(a). The Examiner is respectfully requested to reconsider and withdraw the rejections in view of the amendments and remarks contained herein.

Amendments to Claims

Applicants have amended claims 1, 4, 23 and 26 and canceled claims 3, 25 and 28-46 in this Amendment B. In particular, claims 1 and 23 have been amended to incorporate the limitations of claims 3 and 25 respectively. Claims 4 and 26 have been amended to be dependent from claims 1 and 23 because of the cancellation of claims 3 and 25. Claim 23 has also been amended to further define the method of the invention as a "method of treating or preventing a COX-2 mediated ophthalmic disease or disorder." No new matter has been added. Support for amended claim 23 can be found in the specification, for example, at paragraph [0001]. Upon entry of this Amendment B, claims 1, 4-5, 8-9, 12-24 and 26-27 will be pending in the application.

Rejection under 35 U.S.C. §112

Claims 23-27 stand rejected under 35 U.S.C. §112, first paragraph for failing to comply with the written description requirement. Reconsideration and withdrawal of the rejection is requested in view of the amendments to claim 23 described above. In particular, Applicants have amended claim 23 to be directed to a "method of preventing or treating a COX-2 mediated ophthalmic disease or disorder." Accordingly, the rejection under 35 U.S.C. §112, first paragraph is traversed.

Rejection under 35 U.S.C. § 103(a)

Claims 1-5, 9, and 12-27 stand rejected under 35 U.S.C. §103(a) as being unpatentable over WO 00/25771 in view of Davis et al. and Mazuel et al. Reconsideration and withdrawal of the rejection is requested for the reasons set forth below.

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The present invention provides for opthalmically acceptable formulations of a selective cyclooxygenase-2 (COX-2) inhibitory drug of low water solubility and methods for treating COX-2 mediated ophthalmic diseases or disorders using such formulations. For example, as defined in amended claim 1, a composition of the present invention comprises a selective COX-2 inhibitory drug or a salt or prodrug thereof in a concentration effective for treatment and/or prophylaxis of a COX-2 mediated ophthalmic disorder, and at least one opthalmically acceptable excipient ingredient that reduces the rate of removal of the composition from the eye by lacrimation such that the composition has an effective residence time of about 2 to about 24 hours when topically administered to the eye of a patient. The composition is further defined as being in the form of an in situ gellable solution, suspension or solution/suspension having opthalmically compatible pH and osmolality and containing a carrageenan.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the teachings of prior art references; and the references, when combined, must teach all of the claim limitations. See MPEP 2143. Further, the prior art or knowledge generally available in the art must provide a reasonable expectation of success and the teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on applicant's disclosure. See Id.; In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The principal reference, WO 00/25771 (as described at paragraphs [0026] and [0027] of the specification), describes ophthalmic compositions comprising a prostaglandin analog such as latanoprost and an anti-inflammatory agent. The anti-inflammatory agent is said to reduce iridial pigmentation during topical prostaglandin therapy for glaucoma. Nothing in the reference teaches or suggests an opthalmically acceptable composition comprising a selective COX-2 inhibitory drug. Further, nothing in the reference teaches or suggests the unique problems of formulating an opthalmically acceptable composition which can provide continuous delivery to the eye of a low-water solubility drug such as a selective COX-2 inhibitor as defined by the present invention. Accordingly, Applicants submit that the principal reference fails to provide sufficient suggestion or motivation of the present invention to establish a *prima facie* case of obviousness.

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Further, it is respectfully submitted that the deficiencies of the primary reference cannot be overcome by resort to the teachings of Davis et al. (U.S. Patent No. 5,192,535) or Mazuel et al. (U.S. Patent No. 4,861,760). Davis et al. describe liquid compositions said to be suitable for use as eye drops. See paragraph [0020] of the specification. Upon placement of the composition in the eye, contact with lacrimal fluid having a pH of about 7.2 to about 7.4 is said to result in gelling permitting sustained release of a drug contained in the composition. However, nothing in the reference teaches or suggests the use of selective COX-2 inhibitory drugs or carrageenan as required by the present invention or whether a drug of low water solubility such as the COX-2 drugs of the present invention would be suitable for use in the sustained release compositions described. Accordingly, Applicants submit that the Davis reference fails to provide the required suggestion or motivation which would lead one skilled in the art to practice the present invention.

Mazuel et al. describe a liquid in situ gelling composition said to be suitable for ophthalmic use. See paragraph [0016] of the specification. The composition contains a polysaccharide in aqueous solution that undergoes liquid-gel phase transition in response to ionic strength of tear fluid. However, like Davis et al. described above, nothing in the reference remotely teaches or suggests the use of a selective COX-2 inhibitory drug or carrageenan as required by the present invention. Accordingly, it is respectfully submitted that Mazuel et al. fail to provide any relevant teaching which would lead one skilled in the art to practice the present invention.

Because none of the cited references, either alone or in combination, teach the use of the selective COX-2 inhibitory drugs described in the present invention or their use in an opthalmically acceptable composition which can continuously provide the drug to the eye for a period of at least 2 hours, Applicants respectfully submit that a *prima facie* case of obviousness has not been established with respect to the present invention. Thus, reconsideration and withdrawal of the rejection of claims 1-5, 9 and 12-27 under 35 U.S.C. §103(a) is requested.

Conclusion

It is believed that the present application is in condition for allowance. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes

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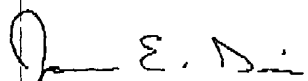
that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (314) 446-7683.

The Commissioner is hereby authorized to charge $950.00 for the purchase of a three-month extension of time under 37 C.F.R. 1.136(a) to Deposit Account No. 08-0750. Further, if there is any other fee deficiency or overpayment of any fees in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or credit such overpayment to Deposit Account No. 08-0750.

Respectfully submitted,



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